Kaufman teaches that retroviral vectors are efficient vehicles for introducing recombinant genetic material into mammalian cells. Kaufman also discusses the advantage of retroviral vectors which allows selection of stable transformants when the retroviruses reverse transcribe their RNA genome into DNA and become integrated into the host genome. However, Kaufman does not suggest or teach the construction of retroviral libraries encoding random peptides.

In contrast, the claimed invention involves retroviral libraries that encode random peptides.

As outlined in M.P.E.P. §2142, a *prima facie* case of obviousness requires that three criteria bet met. First, there must be some suggestion or motivation to combine the references and practice the invention. Secondly, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all of the claim limitations.

Neither Kaufman nor Mirabelli, taken alone or in combination, teach or suggest the creation of retroviral libraries encoding randomized peptides. Mirabelli is drawn to antisense constructs. Kaufman does not teach libraries or random libraries.

The Examiner states that Kaufman provides motivation since stable cell lines may be produced. The applicant respectfully submits that this sentence is taken out of context; the same paragraph outlines:

> However, in general, protein expression from retroviral-based vectors has been low due to problems with RNA spicing and mRNA translation. Since it is unknown which viral DNA sequences are essential for efficient expression in retroviral-based vectors, and since the insertion of different DNA sequence may impair propagation or expression of the recombinant retrovirus, success with these vectors has been variable. (See first paragraph on page 495).

Thus, the applicant submits that Kaufman does not motivate one of skill in the art to combine the references.

Accordingly, a *prima facie* case of obviousness has not been met and the rejection should be withdrawn.

Even assuming, *arguendo*, that the references are combined, there is no reasonable expectation of success that retroviral libraries encoding random peptides could be made.

Furthermore, the cited prior art does not teach or suggest all of the claim limitations. Neither reference teaches or suggests random peptides.

Accordingly, a *prima facie* case of obviousness has not been met and the rejection should be withdrawn.

Claims 16-26 and 28 are rejected as obvious over Mirabelli *et al.* in view of Kaufman and Nillsson *et al.*

Mirabelli and Kaufman are discussed above.

Nillsson suggests the use of fusion proteins in several different embodiments. These include the following: (1) enhance solubility and proper folding of a fused protein; (2) permit efficient purification of a recombinantly generated protein; (3) limit proteolytic degradation and increase in vivo half life of a protein of interest; and (4) use as immunogens to generate antibodies against the fusion protein. Nillsson, however, does not teach or suggest retroviral libraries encoding random peptides.

As outlined above, a *prima facie* case of obviousness requires three criteria be met: (1) there must be motivation to combine the references; (2) there must be a reasonable expectation of success; and (3) all the elements of the claims must be found in the prior art.

None of the cited references, taken alone or in combination, teaches or suggests the creation of retroviral libraries encoding randomized peptides. Mirabelli is drawn to antisense constructs. Kaufman does not teach libraries or random libraries. Nillsson does not teach or suggest retroviral libraries encoding random peptides.

The Examiner states that Nillsson motivates one of skill in the art to practice the invention due to the fact that Nillsson teaches that fusion proteins can be constructed for a variety of reasons. However, even assuming, *arguendo*, that this is true, this does not motivate one of skill in the art to utilize fusion partners with random peptide constructs.

Accordingly, a *prima facie* case of obviousness has not been met and the rejection should be withdrawn.

In addition, the cited prior art does not teach or suggest all of the claim limitations. None of the references teach or suggest random peptides, with or without fusion partners.

Therefore, Applicants respectfully submit that the references, either alone or in combination, do not support a conclusion of obviousness under 35 U.S.C. § 103(a) and respectfully request withdrawal of the rejection.

## CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

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APPENDIX

16. A molecular library of retroviruses comprising at least $10^4$ different randomized nucleic acids encoding a plurality of randomized peptides.

17. A molecular library of retroviruses according to claim 16 comprising at least $10^5$ different randomized nucleic acids encoding a plurality of randomized peptides.

18. A molecular library of retroviruses according to claim 16 comprising at least $10^6$ different randomized nucleic acids encoding a plurality of randomized peptides.

19. A molecular library of retroviruses according to claim 16 comprising at least $10^7$ different randomized nucleic acids encoding a plurality of randomized peptides.

20. A molecular library of retroviruses according to claim 16 comprising at least $10^8$ different randomized nucleic acids encoding a plurality of randomized peptides.

21. A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least $10^4$ different randomized nucleic acids encoding a plurality of randomized peptides.

22. A cellular library according to claim 21 wherein said constructs are integrated into the cellular genome.

23. A molecular library of retroviruses according to claim 16, wherein said nucleic acids further encode a fusion partner.

24. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a targeting sequence.

25. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a rescue sequence.

26. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a stability sequence.

27. A molecular library of retroviruses according to claim 23, wherein said fusion partner comprises a dimerization sequence.

28. A molecular library of retroviruses according to claim 16, wherein said randomized nucleic acids are biased in their randomization.